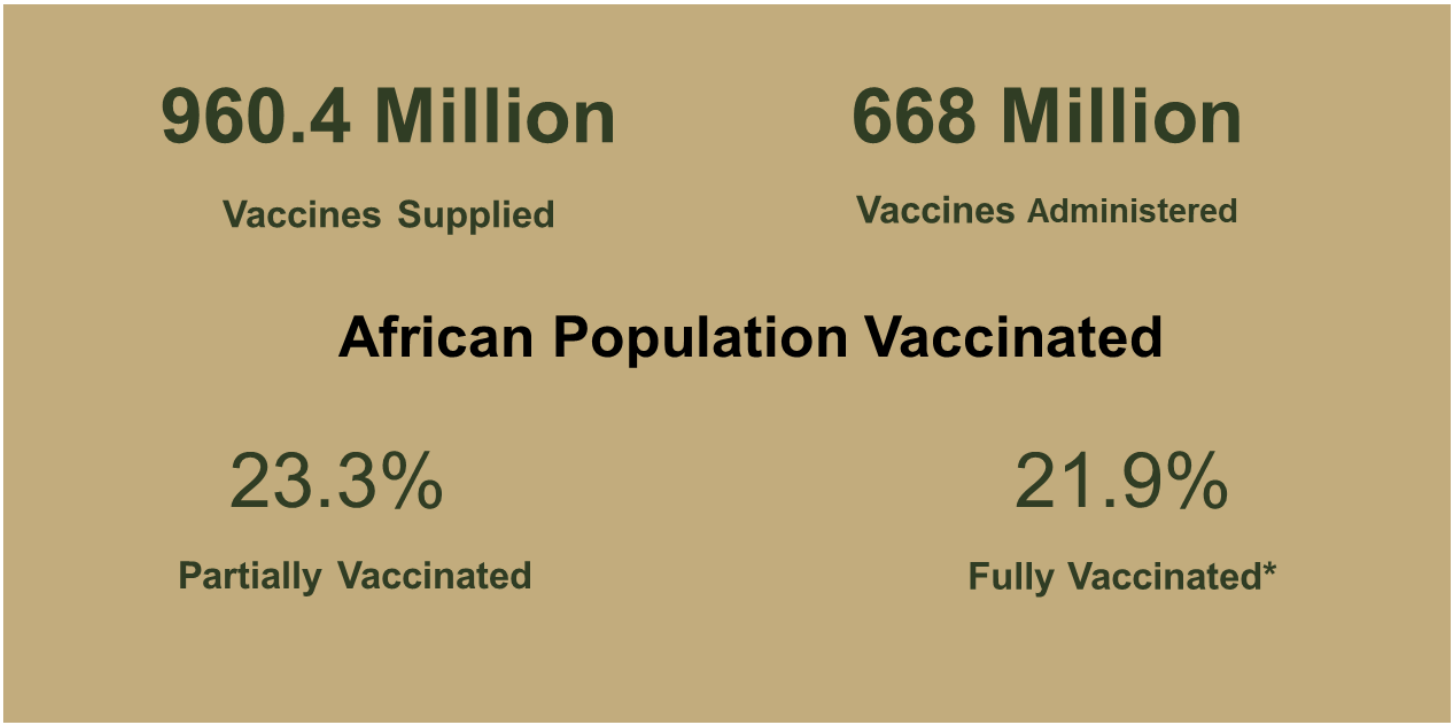
COVID-19 Scientific and Public Health Policy Update[1] (17 August 2022)

This bi-weekly brief details the latest developments in scientific knowledge and public health policy from around the world as well as updates to the COVID-19-related guidance from Africa CDC, WHO and other public health agencies. This brief complements the Weekly Outbreak Brief and other documents on COVID-19 and the actions that the African Union/Africa CDC and WHO/AFRO are taking to help African Union Member States. Contents are ***not intended to serve as recommendations*** *from the African Union-Africa CDC or WHO/AFRO; rather, the brief serves as a summary of the scientific information available in the public space to Member States. The outbreak is evolving rapidly and the nature of this information will continue to change. We will provide regular updates to ensure Member States are informed of the most critical developments on the science and public health best practices related to COVID-19.*

A. Trending Topics

Status of Vaccines in Africa



*Received two doses of a two-dose COVID-19 vaccine series or one dose of the Johnson & Johnson vaccine
https://africacdc.org/COVID-19-vaccination/
Updated 17 August 2022

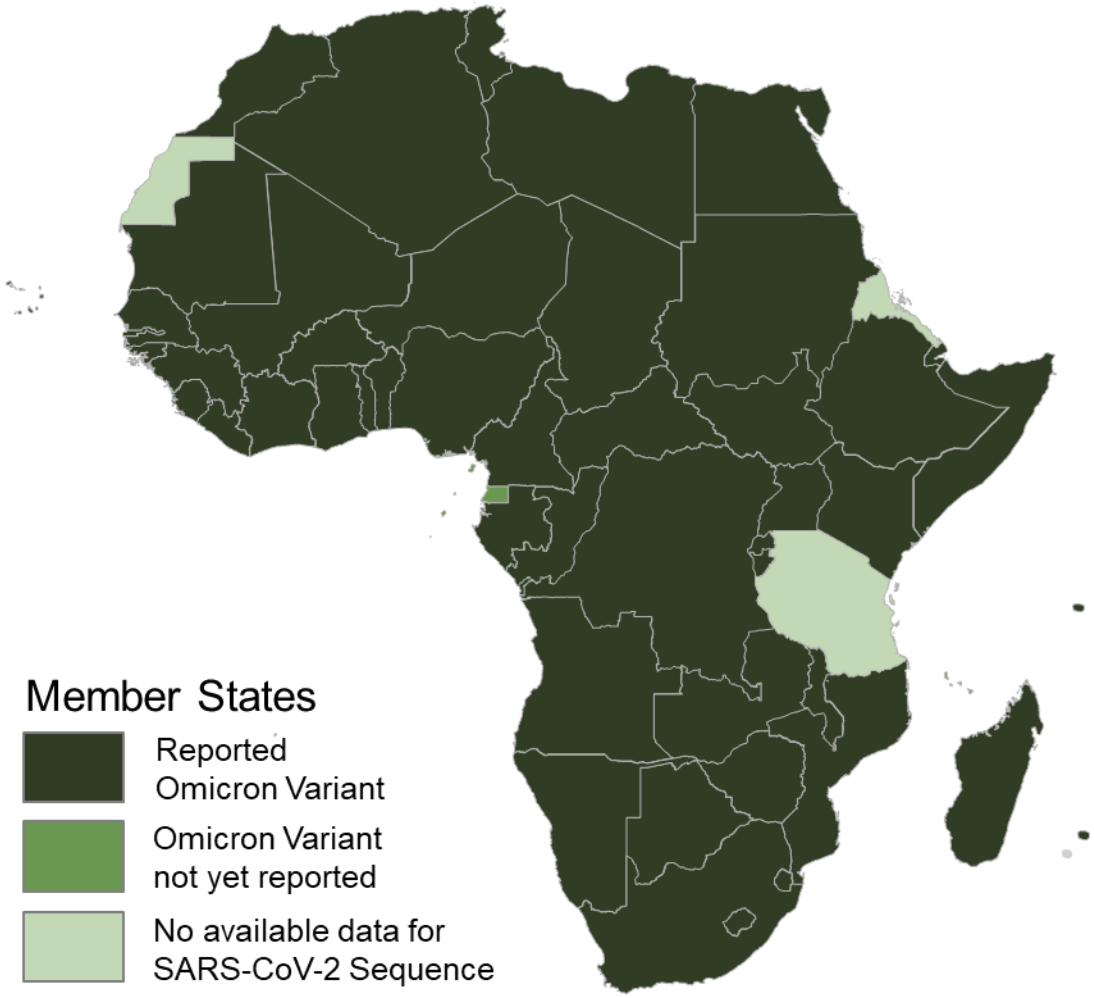
Note: Africa CDC has changed the denominator of the calculation for percentage fully vaccinated from 2020 population to 2022 population estimates (UNFPA) to give accurate projections from effective population size (Ne) perspectives.

The resulting effect is that there will be a slight reduction in fully vaccinated coverage percentages of member states and the continent at large.

[1] This update compiled for use by African Union Member States and is developed collaboratively by the African Union-Africa CDC and World Health Organization - Regional Office for Africa. **This is a preliminary summary of information and does not represent policy decisions, recommendations, or final conclusions of the African Union- Africa CDC or WHO/AFRO**.

Variants of Concern (VOC)

The Omicron variant (B.1.1.529), first reported in South Africa on 24th November 2021, has spread to 198 countries/territories/areas worldwide. As of 17 August 2022, 51 (92.7%) of the 55 Member States in Africa have reported this variant. For more information visit https://africacdc.org/institutes/africa-pathogen-genomics-initiative/.



Updated 17 August 2022

B. New guidelines and resources

Since 2 August 2022,

- Africa CDC[2] has published new guidance and resources on:
  - Outbreak Brief 134: Coronavirus Disease 2019 (COVID-19) Pandemic
  - Revised COVID-19 Testing Strategy, Second Edition, June, 2022

- U.S. CDC[3] has published new guidance and resources on:
  - Selected Adverse Events Reported after COVID-19 Vaccination
  - CDC streamlines COVID-19 guidance to help the public better protect themselves and understand their risk

[2] Africa CDC: Africa Centres for Disease Control and Prevention
[3] U.S. CDC: United States Centres for Disease Control and Prevention

- Isolation and Precautions for People with COVID-19
- Operational Guidance for K-12 Schools and Early Care and Education Programs to Support Safe In-Person Learning
- Summary of Guidance for Minimizing the Impact of COVID-19 on Individual Persons, Communities, and Health Care Systems — United States, August 2022

- WHO[4] has published new guidance and resources on:
  - Safety and monitoring for patients receiving Nirmatrelvir-ritonavir for COVID-19
  - Nirmatrelvir-ritonavir for COVID-19
  - Administration of Molnupiravir for COVID-19
  - Implications of the COVID-19 pandemic for patient safety: a rapid review
  - Administration of Nirmatrelvir-ritonavir for COVID-19
  - Remdesivir for COVID-19
  - Administration of Remdesivir for COVID-19
  - Safety and monitoring in patients receiving remdesivir for COVID-19
  - Safety and monitoring for patients receiving Molnupiravir for COVID-19
  - Molnupiravir for COVID-19
  - Implementation guide for vaccination of health workers

- U.S. FDA[5] has issued press releases on:
  - As of 16 August, 439 tests and sample collection devices are authorised by the FDA under emergency use authorisations (EUAs)
  - On 12 August, FDA issued a safety communication advising people to perform repeat, or serial, testing following a negative result on any at-home COVID-19 antigen test

- ECDC[6] has issued new resources on:
  - Communicable disease threats report, 7-13 August 2022, week 32
  - Methods for the detection and characterisation of SARS-CoV-2 variants - second update

- UKHSA[7] has issued new guidance and press releases on:
  - JCVI publishes advice on COVID-19 vaccines for autumn booster programme
  - Flu immunisation training recommendations
  - Consensus statements and medium-term projections on COVID-19

C. Scientific updates

Basic Science

- This study in South Africa assessed the degree of escape of Omicron BA.4 and BA.5 sub-lineages from neutralising immunity in people previously infected with Omicron BA.1 and determined the effect of vaccination on immune escape using live viral isolates. In BA.1-infected unvaccinated individuals, neutralisation relative to BA.1 declines 7.6-fold for BA.4 and 7.5-fold for BA.5. In vaccinated individuals with subsequent BA.1 infection, neutralisation relative to BA.1 decreases 3.2-fold for BA.4 and 2.6-fold for BA.5. The fold-drop versus ancestral virus neutralisation in this group is 4.0-fold for BA.1, 12.9-fold for BA.4, and 10.3-fold for BA.5. In contrast, BA.4/BA.5 escape is similar to BA.1 in the absence of BA.1 elicited immunity: fold-drop relative to ancestral virus neutralisation is 19.8-fold for BA.1, 19.6-fold for BA.4, and 20.9-fold for BA.5. These results show considerable escape of BA.4/BA.5 from BA.1

[4] WHO: World Health Organization
[5] U.S. FDA: United States Food and Drug Administration
[6] ECDC: European Centre for Disease Prevention and Control
[7] UKHSA: United Kingdom Health Security Agency

elicited immunity which is moderated with vaccination and may indicate that BA.4/BA.5 may have the strongest selective advantage in evading neutralisation relative to BA.1 in unvaccinated, BA.1 infected individuals.

- This study in the United States developed a novel method for detecting recombination in pandemic-scale phylogenies. The authors used the novel method to search a nearly comprehensive SARS-CoV-2 phylogeny for recombinant lineages. In a 1.6M sample tree from May 2021, they identified 589 recombination events, which indicate that approximately 2.7% of sequenced SARS-CoV-2 genomes have detectable recombinant ancestry. Recombination breakpoints are inferred to occur disproportionately in the 3' portion of the genome that contains the spike protein. Their results highlight the need for timely analyses of recombination for pinpointing the emergence of recombinant lineages with the potential to increase transmissibility or virulence of the virus. The authors anticipate that this approach will empower comprehensive real time tracking of viral recombination during the SARS-CoV-2 pandemic and beyond.
- This study in the United States evaluated SARS-CoV-2 variants of concern (VOCs) binding, cross-inhibition, and neutralisation potency of 73 monoclonal antibodies from donors infected in early 2020 with ancestral SARS-CoV-2. The authors identified three antibodies that neutralised all VOCs tested (including Omicron BA.1) and used cryogenic electron microscopy (cryo-EM) of these antibodies bound with SARS-CoV-2 spike to suggest ways in which somatic mutation might restore VOC recognition by other antibodies. This study thus yields better understanding of the reactivity for VOCs of humoral immune responses to ancestral SARS-CoV-2.
- This study in Germany assessed levels of autoantibodies against three neuronal antigens that are hypothesised to underlie the severe respiratory failure in COVID-19 patients with neurological complications. Microarrays were used to screen serum from COVID-19 patients admitted to intensive care (n=23) and compared those with controls (n=16) who experienced mild course of the disease. The authors had previously identified three brainstem-related proteins: disabled-homolog-1 (DAB1), mitochondrial apoptosis inducing factor 1 (AIFM1) and surfeit-locus-protein-1(SURF1). The results confirm the occurrence of IgG and IgM antibodies against the hypothesised epitopes in COVID-19 patients. Importantly, while IgM levels were similar in both groups, IgG levels were significantly elevated in severely ill patients compared to controls, suggesting a pathogenic role of IgG. The newly discovered anti-neuronal antibodies might be promising markers of severe disease and the targeted peptide epitopes might be used for targeted immunomodulation.

Vaccines

- This national cohort study in Singapore assessed the effectiveness of partial and full vaccination with the BNT162b2 vaccine against the omicron variant in children 5 to 11 years of age. The study involved 255,936 children from 21 January through 8 April 2022. Among unvaccinated children, the crude incidence rates of all reported SARS-CoV-2 infections, PCR-confirmed SARS-CoV-2 infections, and COVID-19–related hospitalisations were 3303.5, 473.8, and 30.0 per 1 million person-days, respectively. Among partially vaccinated children, vaccine effectiveness was 13.6% (95% CI, 11.7 to 15.5) against all SARS-CoV-2 infections, 24.3% (95% CI, 19.5 to 28.9) against PCR-confirmed SARS-CoV-2 infection, and 42.3% (95% CI, 24.9 to 55.7) against COVID-19–related hospitalisation; in fully vaccinated children, vaccine effectiveness was 36.8% (95% CI, 35.3 to 38.2), 65.3% (95% CI, 62.0 to 68.3), and 82.7% (95% CI, 74.8 to 88.2), respectively.
- This observational cohort study in Canada assessed the frequency and nature of significant health events among pregnant females after COVID-19 vaccination. The study included 5,625 pregnant, vaccinated females aged 15–49 years, compared with 185,735 non-pregnant vaccinated females and 339 pregnant unvaccinated controls of a similar age. Overall, 226 (4.0%) of 5,597 vaccinated pregnant females reported a significant health event after dose one of an mRNA vaccine, and 227 (7.3%) of 3,108 after dose two, compared with 11 (3.2%) of 339 pregnant unvaccinated females. Pregnant vaccinated females had an increased odds of a significant health event within 7 days of the vaccine after dose two of mRNA-1273 (adjusted odds ratio [aOR] 4.4 [95% CI 2.4–8.3]) compared with pregnant unvaccinated controls within the past 7 days, but not after dose one of mRNA-1273 or any dose of

BNT162b2. Pregnant vaccinated females had decreased odds of a significant health event compared with non-pregnant vaccinated females after both dose one (aOR 0.63 [95 CI 0.55–0.72]) and dose two (aOR 0.62 [0.54–0.71]) of any mRNA vaccination. There were no significant differences in any analyses when restricted to events which led to medical attention. These findings indicate that COVID-19 mRNA vaccines have a good safety profile in pregnancy.

Diagnostics

- This study in the United States describes the development of an assay for rapid COVID-19 testing and its implementation in a prototype microfluidic device. The assay, which was named DISCoVER (for diagnostics with coronavirus enzymatic reporting), involves extraction-free sample lysis via shelf-stable and low-cost reagents, multiplexed isothermal RNA amplification followed by T7 transcription, and Cas13-mediated cleavage of a quenched fluorophore. The device consists of a single-use gravity-driven microfluidic cartridge inserted into a compact instrument for automated running of the assay and readout of fluorescence within 60 minutes. DISCoVER can detect SARS-CoV-2 in saliva with a sensitivity of 40 copies μl^{-1}, and was 94% sensitive and 100% specific when validated (against quantitative PCR) using total RNA extracted from 63 nasal-swab samples (33 SARS-CoV-2-positive, with cycle-threshold values of 13–35). The device correctly identified all tested clinical saliva samples (10 SARS-CoV-2-positive out of 13, with cycle-threshold values of 23–31).
- This study in the United States describes the development and application of a 3D-printed lab-on-a-chip that concurrently detects, via multiplexed electrochemical outputs and within 2 hours, SARS-CoV-2 RNA in saliva as well as anti-SARS-CoV-2 immunoglobulins in saliva spiked with blood plasma. The device automatedly extracts, concentrates and amplifies SARS-CoV-2 RNA from unprocessed saliva, and integrates the Cas12a-based enzymatic detection of SARS-CoV-2 RNA via isothermal nucleic acid amplification with a sandwich-based enzyme-linked immunosorbent assay on electrodes functionalized with the Spike S1, nucleocapsid and receptor-binding-domain antigens of SARS-CoV-2. Inexpensive microfluidic electrochemical sensors for performing multiplexed diagnostics at the point of care may facilitate the widespread monitoring of COVID-19 infection and immunity.

Care and Treatment

- This prospective, single-centre study in Belgium assessed plasma and tissue kallikrein activity, along with kinins and myeloperoxidase (MPO)-DNA complexes as a biomarker for neutrophil extracellular traps (NETs) in bronchoalveolar lavage (BAL) fluid samples from patients with or without COVID-19 pneumonia. The study involved 43 patients at a tertiary care centre in Leuven between March 2020 and May 2020. BAL fluid from patients with severe COVID-19 (n = 21, of which 19 were mechanically ventilated) was observed to have higher tissue kallikrein activity (18.2 pM [1.2-1535.0], median [range], n = 9 vs 3.8 [0.0-22.0], n = 11; p = 0.030), higher levels of the kinin peptide bradykinin-(1-5) (89.6 [0.0-2425.0], n = 21 vs 0.0 [0.0-374.0], n = 19, p = 0.001), and higher levels of MPO-DNA complexes (699.0 ng/mL [66.0-142621.0], n = 21 vs 70.5 [9.9-960.0], n = 19, p < 0.001) compared to patients without COVID-19. These findings support the hypothesis that dysregulation of the kallikrein-kinin system might occur in mechanically ventilated patients with severe pulmonary disease, which might help to explain the clinical presentation of patients with severe COVID-19 developing pulmonary oedema and thromboembolic complications. Targeting the kallikrein-kinin system should be further explored as a potential treatment option for patients with severe COVID-19.
- This cohort study in the United States assessed the long-term (12 months) cardiovascular outcomes in COVID-19 survivors. The study involved 4,131,717 participants who underwent SARS-CoV-2 testing in a Collaborative Network from 48 healthcare organizations between January 2019 and March 2022. COVID-19 survivors were associated with increased risks of cerebrovascular diseases, such as stroke (HR [95% CI] = 1.618 [1.545-1.694]), arrhythmia related disorders, such as atrial fibrillation (HR [95% CI] = 2.407 [2.296-2.523]), inflammatory heart disease, such as myocarditis (HR [95% CI] =4.406 [2.890-6.716]), ischemic heart disease(IHD), like ischemic cardiomyopathy (HR [95% CI] = 2.811 [2.477-3.190]), other cardiac disorders, such as heart failure (HR [95% CI] =2.296 [2.200-2.396]) and

thromboembolic disorders (e.g. pulmonary embolism: HR [95% CI] =2.648 [2.443-2.870]). The risks of two composite endpoints, major adverse cardiovascular event (HR [95% CI] = 1.871 [1.816–1.927]) and any cardiovascular outcome (HR [95% CI] = 1.552 [1.526–1.578]), were also higher in the COVID-19 survivors than in the controls. The survival probability of COVID-19 survivors dramatically decreased in all the cardiovascular outcomes. The risks of cardiovascular outcomes were evident in both male and female COVID-19 survivors. Furthermore, the risk of mortality was higher in the elderly COVID-19 survivors (age ≥ 65 years) than in the young ones.

Epidemiology

- This prospective, population-based, observational cohort study in the Netherlands assessed the nature, prevalence, and severity of long-term symptoms related to COVID-19, while correcting for symptoms present before SARS-CoV-2 infection and controlling for the symptom dynamics in the population without infection. The study involved 4,231 participants who had COVID-19 and 8,462 controls (matched by age, sex, and time). Persistent symptoms in COVID-19-positive participants at 90–150 days after COVID-19 compared with before COVID-19 and compared with matched controls included chest pain, difficulties with breathing, pain when breathing, painful muscles, ageusia or anosmia, tingling extremities, lump in throat, feeling hot and cold alternately, heavy arms or legs, and general tiredness. In 12.7% of patients, these symptoms could be attributed to COVID-19, as 381 (21.4%) of 1,782 COVID-19-positive participants versus 361 (8.7%) of 4,130 COVID-19-negative controls had at least one of these core symptoms substantially increased to at least moderate severity at 90–150 days after COVID-19 diagnosis or matched timepoint. The authors recommend further research that distinguishes potential mechanisms driving post-COVID-19-related symptomatology.
- This study in Qatar assessed the immune protection of infection with one sub-lineage against reinfection with the other sub-lineage during a large BA.1 and BA.2 Omicron wave (December 2021 to March 2022). Two national matched, retrospective cohort studies are conducted to estimate effectiveness of BA.1 infection against reinfection with BA.2 (N = 20,994; BA.1-against-BA.2 study), and effectiveness of BA.2 infection against reinfection with BA.1 (N = 110,315; BA.2-against-BA.1 study). Effectiveness of BA.1 infection against reinfection with BA.2 is estimated at 94.2% (95% CI: 89.2–96.9%). Effectiveness of BA.2 infection against reinfection with BA.1 is estimated at 80.9% (95% CI: 73.1–86.4%). Infection with the BA.1 sub-lineage appears to induce strong, but not full immune protection against reinfection with the BA.2 sub-lineage, and vice versa, for at least several weeks after the initial infection.
- This cohort study in Belgium assessed the risk of contracting COVID-19 for contacts traced in an extended contact tracing window (5 days [extended] vs 2 days before symptom onset or diagnosis [standard]). The study involved 659 confirmed cases of COVID-19 and 2396 contacts in a university population. Backward contact tracing identified an additional 42% (or 55% in a mathematical model of iterative tracing) of cases not detected through the contact tracing protocol used in most jurisdictions. The main trade-off was that infected backward traced contacts were identified on average 1.8 days later in their infectious cycle than forward traced contacts. However, the burden of testing and quarantine was lower in backward traced contacts due to inherent differences in the timing of their last exposure to the index case. Their results support implementing backward contact tracing when rigorous suppression of viral transmission is warranted.
- This retrospective multicentre cohort study in Brazil evaluated the association between obesity and COVID-19 mortality and length of stay in intensive care unit (ICU) patients, and how these associations were modified by age groups. The study involved 8183 ICU patients across 32 hospitals. Those in the younger group with severe obesity had an increased risk of COVID-19 mortality compared to those with normal/overweight (HR 1.27; 95% CI 1.01–1.61). An increased risk of death was also observed for patients who were underweight (HR 3.74; 95% CI 1.39–10.07). For patients aged ≥ 60 year, mild/moderate obesity was associated with reduced mortality risk (HR 0.87; 95% CI 0.78–0.97). For the age group < 60 years, the length of stay in ICU for those patients with severe obesity was 35% higher compared to the normal/overweight category (e^{β} 1.35; 95% CI 1.21–1.51). Conversely, for the survivors in the underweight category, the length of stay in ICU was 51% lower compared to the

normal/overweight group (e^{β} 0.49; 95% CI 0.31–0.78). In the age group ≥ 60 years, mild/moderate obesity was associated with an increased length of stay in the ICU (e^{β} 1.10; 95% CI 1.01–1.21), adjusting for confounders. These findings could be helpful for health professionals to identify subgroups at higher risk for worse outcomes.

- This cross-sectional study in Nigeria assessed gender differences in health care workers' (HCWs) work attendance under COVID-19 and household burdens as a potential mediator of the gender difference. The study involved 334 HCWs across 16 facilities in the Gombe, Katsina, and Zamfara states in Northern Nigeria. Only 2.10% of HCWs reported <5 days of work in a typical week; 35.33% worked 6-7 days a week (i.e., HCW overwork). Males were more likely than females to report HCW overwork (46.33% vs. 22.93%), and females were more likely than males to report an increase in household burden (59.24% vs. 40.68%). Adjusted regression models found that men were more likely than women to report HCW overwork (ARR: 1.76, 95% CI: 1.17-2.66). Increased household burdens mediated 9% of the total effect between gender and HCW work attendance. The COVID-19 pandemic in Northern Nigeria made female HCWs contend with the dual burdens of formal and informal care work. This contributes to lower attendance among female HCWs and overwork for their male counterparts.

Infection Prevention & Control

- This retrospective cohort study in Israel assessed the real-world effectiveness of REGEN-COV (casirivimab and imdevimab) treatment against COVID-19-related hospitalisation, severe disease, and death. The study compared patients infected with the Delta variant and treated with REGEN-COV (n = 289) to those infected but not-treated with REGEN-COV (n = 1,296). Analysis was performed using Cox regression, with estimated treatment effectiveness defined as one minus the hazard ratio. A subgroup analysis was conducted as a secondary analysis by age group (<60 or ≥60 years old). Treatment effectiveness of REGEN-COV was 56.4% (95% CI: 23.7–75.1%) in preventing COVID-19 hospitalisation, 59.2% (95% CI: 19.9–79.2%) in preventing severe COVID-19, and 93.5% (95% CI: 52.1–99.1%) in preventing COVID-19 death in the 28 days after treatment. These results show that REGEN-COV was effective in reducing the risk of severe sequelae in high-risk COVID-19 patients.

Non-pharmaceutical interventions, social distancing

- This study in the United Kingdom assessed the effectiveness and acceptability of smartphone customised frame technology to improve the fit of disposable filtering facepiece class 3 (FFP3) respirators for dental staff who previously failed fit testing. The study involved 20 volunteers who previously failed FFP3 fit testing. The participants were recruited to use smartphone technology (Bellus3D FaceApp) to have a 3D-printed bespoke face frame produced for them. Fit test passes increased from 5% without the frame to 70% and 95%, respectively, for masks A and B with the frame (p <0.01). Very few participants reported using the technology as difficult (n = 1/20) or the frame uncomfortable (n = 3/20) or difficult to wear (n = 0/20).
- This observational cohort study in South Korea assessed the association of changing public health and social measures (PHSMs) with the transmissibility of the Omicron variant. The study utilised data on the daily number of laboratory-confirmed COVID-19 local cases by polymerase chain reaction test or rapid antigen test results and the proportion of Omicron cases during the early phase of the Omicron (lineage BA.1) wave: 1 December 2021 to 16 March 2022. The time-varying effective reproduction number, R_t, which represents the mean number of infections resulting from a case infected at time *t,* was sustained at greater than 1 during the study period. The relaxation of restrictions for social gatherings and suspension of the need for vaccine passes were associated with increases in R_t of 20.4% (95% CI, 5.8%-36.5%) and 10.9% (3.2%-24.8%), respectively. However, extending community COVID-19 screening centres and mandatory COVID-19 screening for all students in schools were associated with reductions in R_t of −16.8% (−25.2% to −11.1%) and −18.8% (−22.2% to −11.1%), respectively.

D. Clinical Trials Updates

Key updates:

Vaccine trials:

- On 15 August 2022, Moderna announced the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK has granted conditional authorization for the use of the Omicron-containing bivalent COVID-19 booster vaccine, mRNA-1273.214 as a booster dose for active immunization to prevent COVID-19 in individuals 18 years of age and older. Spikevax Bivalent Original/Omicron (mRNA-1273.214) is a next-generation bivalent vaccine that contains mRNA-1273 (Spikevax) and a vaccine candidate targeting the Omicron variant of concern (BA.1). The decision based on clinical trial data from a phase 2/3 trial, in which mRNA-1273.214 met all primary endpoints, including superior neutralising antibody response against Omicron (BA.1) when compared to a 50-µg booster dose of mRNA-1273 in baseline seronegative participants. A booster dose of mRNA-1273.214 increased neutralising geometric mean titres (GMT) against Omicron approximately 8-fold above baseline levels. In addition, mRNA-1273.214 elicited potent neutralising antibody responses against the Omicron subvariants BA.4 and BA.5 compared to the currently authorized booster (mRNA-1273) regardless of prior infection status or age. Clinical trial registration #: (NCT05249829).
- On 15 August 2022, Novavax announced the submission of an application to the U.S. Food and Drug Administration (FDA) for Emergency Use Authorization (EUA) of its protein-based COVID-19 Vaccine, Adjuvanted for active immunization to prevent COVID-19 as a homologous and heterologous booster in adults aged 18 and older. The application is supported by data from Novavax' Phase 3 PREVENT-19 trial conducted in the United States and Mexico, and from the UK-sponsored COV-BOOST Phase 2 trial. As part of an open-label booster phase of the PREVENT-19 trial, a single booster dose of the Novavax COVID-19 Vaccine, Adjuvanted was administered to healthy adult participants at least six months after their primary two-dose vaccination series of the Novavax COVID-19 Vaccine, Adjuvanted. The third dose produced robust antibody responses comparable to or exceeding levels associated with the efficacy data in the primary series Phase 3 clinical trials. In the COV-BOOST trial, the Novavax COVID-19 Vaccine, Adjuvanted induced a significant antibody response when used as a heterologous third booster dose. Following the booster, local and systemic reactions had a median duration of approximately two days. Safety reporting of reactogenicity events showed an increasing incidence across all three doses of the Novavax COVID-19 Vaccine, Adjuvanted, reflecting the increased immunogenicity seen with a third dose. Medically attended adverse events, potentially immune-mediated medical conditions, and severe adverse events occurred infrequently following the booster dose. Clinical trial registration #: (NCT04611802).
- On 12 August 2022, Novavax announced SK bioscience has received a Post Approval Change Application approval from Korean Ministry of Food and Drug Safety (KMFDS) for Nuvaxovid (NVX-CoV2373) COVID-19 vaccine for active immunization to prevent COVID-19 in adolescents aged 12 through 17. The approval was based on data from the ongoing paediatric expansion of the Phase 3 PREVENT-19 trial of 2,247 adolescents aged 12 through 17 years across 73 sites in the U.S., to evaluate the safety, effectiveness (immunogenicity), and efficacy of Nuvaxovid. In the trial, Nuvaxovid achieved its primary effectiveness endpoint and demonstrated 80% clinical efficacy overall at a time when the Delta variant was the predominant circulating SARS-CoV-2 strain in the U.S. Clinical trial registration #: (NCT04611802).
- On 10 August 2022, Novavax announced the Thailand Food and Drug Administration (Thai FDA) has granted expanded emergency use authorization (EUA) for Novavax' protein-based vaccine for active immunization to prevent COVID-19 in adolescents aged 12 through 17. The expanded EUA is based on data from the ongoing paediatric expansion of the Phase 3 PREVENT-19 trial of 2,247 adolescents aged 12 through 17 years across 73 sites in the U.S., to evaluate the safety, effectiveness (immunogenicity), and efficacy of the Novavax COVID-19 vaccine. In the trial, the vaccine achieved its primary effectiveness endpoint and demonstrated 80% clinical efficacy overall at a time when the Delta variant was the predominant circulating SARS-CoV-2 strain in the U.S. Preliminary safety data from the trial showed that serious and severe adverse events were low in number and balanced between vaccine and placebo groups, and not considered related to the vaccine. Local and systemic reactogenicity was generally lower than or similar to adults, after the first and second dose. No new

safety signal was observed through the placebo-controlled portion of the study. Clinical trial registration #: (NCT04611802)

- On 4 August 2022, Novavax announced the initiation of its Phase 2b/3 Hummingbird global clinical trial. The trial will evaluate the safety, effectiveness (immunogenicity), and efficacy of two doses of the Novavax COVID-19 vaccine (NVX-CoV2373) in younger children aged six months through 11 years, followed by a booster at six months after the primary vaccination series. The trial will seek to enrol 3,600 participants in the US, Mexico, Colombia, Argentina, Spain, UK, South Africa, Philippines, and Brazil. Clinical trial registration #: (NCT05468736).
- On 3 August 2022, Sinovac Biotech announced the Health Bureau of the Government of the Hong Kong Special Administrative Region of the People's Republic of China has approved the CoronaVac COVID-19 vaccine intended for children aged 6 months to 3 years. The approval based on related clinical trials and studies of vaccination for local children and adolescents. The phase 3 clinical studies among children aged 6 months to 17 years preliminary results show the vaccine has a good safety and immunogenicity profile, with no severe adverse reaction reported 6 months after two doses of vaccination among children aged 6 months to 35 months. The vaccination schedule for this age group follows the same vaccination schedule of older children. Three doses of vaccines will be used for children aged six months to under three years of age, with the first two doses given 28 days apart followed by a third dose at least 3 months after the second dose, and there is no restriction on the application for immunosuppressed children. Clinical trial registration #: (NCT04992260)

Therapeutics trials:

- On 15 August 2022, Virios Therapeutics announced commencement of enrolment in its exploratory Long-COVID trial. The trial will assess the safety and effectiveness of antiviral therapy with Virios' second development combination, IMC-2 (valacyclovir + celecoxib), to treat the symptoms associated with Long-COVID, including fatigue, pain, sleep disruption, anxiety, depression and cognitive function and overall health improvement. IMC-2 is a novel, dual mechanism antiviral therapy combining valacyclovir and celecoxib designed to synergistically suppress herpes virus activation and replication, with the end goal of reducing viral mediated disease burden.
- On 4 August 2022, Ascletis announces its Investigational New Drug (IND) application of ASC10, an oral inhibitor drug candidate targeting RNA-dependent RNA polymerase (RdRp) for COVID-19 has been accepted by China National Medical Products Administration (NMPA). ASC10 is an orally bioavailable double prodrug which has a new and differentiated chemical structure from the single prodrug molnupiravir. After oral administration, both ASC10 and molnupiravir are rapidly and completely converted in vivo into the same active metabolite ASC10-A, also known as β-D-N4-hydroxycytidine (NHC).
- On 3 August 2022, Ascletis announces the U.S. Food and Drug Administration (FDA) has approved its Investigational New Drug (IND) application for ASC10, an oral drug candidate targeting RNA-dependent RNA polymerase (RdRp) for COVID-19, to conduct the Phase Ib clinical trial in mild-to-moderate COVID-19 patients. Ascletis will immediately initiate the clinical trial in patients to collect ASC10's clinical safety, pharmacokinetics and preliminary efficacy data. ASC10 is an orally bioavailable double prodrug which has a new and differentiated chemical structure from the single prodrug molnupiravir. After oral administration, both ASC10 and molnupiravir are rapidly and completely converted in vivo into the same active metabolite ASC10-A, also known as β-D-N4-hydroxycytidine (NHC). ASC10 was discovered and developed in-house. In SARS-CoV-2 infected mouse models, ASC10 at 240 mg/kg twice daily led to a 4.0 log reduction in viral titre in lungs, equivalent to molnupiravir at 500 mg/kg twice daily. Preclinical studies demonstrated that ASC10-A has potent cellular antiviral activity against Omicron variant (EC50 = 0.3 μM), Delta variant (EC50 = 0.5 μM) and wildtype virus (EC50 = 0.7 μM). It also suggested that there were no drug-drug interactions between ASC10 and other common medicines. FDA recommended the first clinical study of ASC10 to be conducted in mild-to-moderate COVID-19 patients rather than in healthy subjects. The study is a randomized, placebo-controlled Phase Ib clinical trial to determine the safety, tolerability, pharmacokinetics and preliminary efficacy in multiple ascending doses of ASC10 tablets (200 mg, 400

mg or 800 mg twice daily) in mild-to-moderate COVID-19 patients for 5.5-day treatment with 28-day monitoring.

Immunotherapies trials:

- On 8 August 2022, Frontier Biotechnologies announced positive results from the Phase 1 clinical trial of its drug candidate, FB2001 – a small molecule inhibitor of coronavirus main protease (Mpro) – in healthy adult volunteers. A total of 120 participants (80 Whites in the US and 40 Chinese in China) received intravenous infusions of FB2001 at either single doses from 5 mg to 400 mg, or multiple doses of 30 mg to 400 mg daily for 5 days. The data showed FB2001 to be safe and well tolerated among trial participants. Adverse events reported during the trial were mostly mild-to-moderate in severity, with no significant differences observed between participants in the Chinese and American study centres. Clinical trial registration #: (NCT05197179).

Contributors

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